

A LISTING OF THE CLAIMS

1. (Currently amended) A cell growth apparatus comprising a cell growth chamber having an interior side and an exterior side and comprising a wall and a base defining an interior volume, the cell growth chamber comprising an elastomeric growth substrate comprising an elastomeric membrane of a first material ~~that comprises a first portion having a first elasticity and a second portion having a second elasticity~~ defining a three-dimensional cell strain surface having an elasticity differential that comprises one of (i) an elastic modulus differential between a first portion and a second portion of the first material and (ii) a surface feature differential between the first and second portions, the elastomeric membrane having one or more engineered structural formations integrated therewith for receiving and growing cells.
2. (Withdrawn) The apparatus of claim 1, wherein at least a portion of the base of the cell growth chamber consists of the elastomeric growth substrate.
3. (Withdrawn) The apparatus of claim 2, further comprising a secondary chamber in fluid connection with and partially defined by an exterior side of the elastomeric growth substrate, the secondary chamber comprising an opening having a fitting for a pipe or tube.
4. (Withdrawn) The apparatus of claim 3, further comprising a pump in fluid communication with the secondary chamber.
5. (Withdrawn) The apparatus of claim 1, wherein the elastomeric membrane has a portion of a first thickness, having a first elasticity, and a portion of a second thickness, having a second elasticity.
6. (Withdrawn) The apparatus of claim 1, wherein a second material having a different elasticity than the first material is embedded within or attached to the elastomeric membrane.
7. (Withdrawn) The apparatus of claim 6, wherein the second material is one of a polymer, a metal, a ceramic and a fabric.
8. (Withdrawn) The apparatus of claim 7, wherein the second material is a nylon mesh.

9. (Withdrawn) The apparatus of claim 7, wherein the second material is a stainless steel mesh.
10. (Withdrawn) The apparatus of claim 1, wherein the substrate further comprises one or more additional elastomeric layers, at least one of which is attached to the elastomeric membrane.
11. (Withdrawn) The apparatus of claim 10, wherein one or more of the additional elastomeric layer is biodegradable.
12. (Withdrawn) The apparatus of claim 11, wherein the biodegradable layer comprises a poly(glycerol-sebacate) polymer.
13. (Original) The apparatus of claim 1, wherein the interior side of the elastomeric membrane is partially or fully coated with an extracellular matrix-mimetic.
14. (Original) The apparatus of claim 13, wherein the extracellular matrix mimetic is selected from the group consisting of fibronectin, vitronectin, collagen, laminin, poly(lactide) , poly(lactide-co-glycolide) and a self-complementary oligopeptide matrix.
15. (Original) The apparatus of claim 13, where in the extracellular matrix mimetic is fibronectin.
16. (Original) The apparatus of claim 13, wherein the extracellular matrix mimetic partially coats the interior side of the elastomeric membrane.
17. (Original) The apparatus of claim 16, further comprising an adhesion inhibitor covering parts of the interior side of the elastomeric membrane not covered by the extracellular matrix mimetic.
18. (Original) The apparatus of claim 17, wherein the adhesion inhibitor is one of bovine serum albumin and a poly(ethylene oxide)/ poly(propylene oxide)/ poly(ethylene oxide) triblock polymer.

19. (Withdrawn) The apparatus of claim 1, wherein the first portion has a first elastic modulus and the second portion has a second elastic modulus.
20. (Withdrawn) The apparatus of claim 1, wherein the membrane comprises one or more internal passageways.
21. Cancelled.
22. (Withdrawn and currently amended) The apparatus of claim 1 [[21]], wherein the engineered structural formation is one of a surface groove and a passageway within the membrane.
23. (Withdrawn) The apparatus of claim 22, wherein the surface groove or passageway within the membrane has a diameter of less than 100 μ .
24. (Withdrawn) The apparatus of claim 22, wherein the membrane comprises an internal passageway that opens into the interior volume.
25. (Withdrawn) The apparatus of claim 22 wherein the passageway is coated with an extracellular matrix mimetic.
26. (Withdrawn) The apparatus of claim 1, wherein the elastomeric membrane is biodegradable.
27. (Withdrawn) The apparatus of claim 26, wherein the biodegradable membrane comprises a poly(glycerol-sebacate) polymer.
28. (Withdrawn) The apparatus of claim 1, wherein the wall is annular.
29. (Withdrawn) The apparatus of claim 1, wherein the wall is ellipsoid.
30. (Withdrawn) The apparatus of claim 1, wherein at least a portion of the substrate is coated with an adhesion promoter.

31. (Currently amended) An elastomeric cell growth substrate comprising an elastomeric membrane of a first material that comprises a first portion having a first elasticity and a second portion having a second elasticity defining a three-dimensional cell strain surface having an elasticity differential that comprises one of (i) an elastic modulus differential between a first portion and a second portion of the first material and (ii) a surface feature differential between the first and second portions, the elastomeric membrane having one or more engineered structural formations integrated therewith for receiving and growing cells.
32. (Withdrawn) The substrate of claim 31, wherein the elastomeric membrane has a portion of a first thickness, having a first elasticity, and a portion of a second thickness, having a second elasticity.
33. (Withdrawn) The substrate of claim 31, wherein a second material having a different elasticity than the first material is embedded within or attached to the elastomeric membrane.
34. (Withdrawn) The substrate of claim 33, wherein the second material is one of a polymer, a metal, a ceramic and a fabric.
35. (Withdrawn) The substrate of claim 34, wherein the second material is a nylon mesh.
36. (Withdrawn) The substrate of claim 34, wherein the second material is a stainless steel mesh.
37. (Withdrawn) The substrate of claim 31, wherein the substrate further comprises one or more additional elastomeric layers, at least one of which is attached to the elastomeric membrane.
38. (Withdrawn) The substrate of claim 37, wherein one or more of the additional elastomeric layer is biodegradable.
39. (Withdrawn) The substrate of claim 38, wherein the biodegradable layer comprises a poly(glycerol-sebacate) polymer.

40. (Original) The substrate of claim 31, wherein the interior side of the elastomeric membrane is partially or fully coated with an extracellular matrix-mimetic.
41. (Original) The substrate of claim 40, wherein the extracellular matrix mimetic is selected from the group consisting of fibronectin, vitronectin, collagen, laminin, poly(lactide), poly(lactide-co-glycolide) and a self-complementary oligopeptide matrix.
42. (Original) The substrate of claim 40, where in the extracellular matrix mimetic is fibronectin.
43. (Original) The substrate of claim 40, wherein the extracellular matrix mimetic partially coats the interior side of the elastomeric membrane.
44. (Original) The substrate of claim 43, further comprising an adhesion inhibitor covering parts of the interior side of the elastomeric membrane not covered by the extracellular matrix mimetic.
45. (Original) The substrate of claim 44, wherein the adhesion inhibitor is one of bovine serum albumin and a poly(ethylene oxide)/ poly(propylene oxide)/ poly(ethylene oxide) triblock polymer.
46. (Withdrawn) The substrate of claim 31, wherein the first portion has a first elastic modulus and the second portion has a second elastic modulus.
47. (Withdrawn and currently amended) The substrate of claim 31, wherein the ~~membrane~~ engineered structural formation comprises one or more internal passageways.
48. cancelled.
49. (Withdrawn and currently amended) The substrate of claim 31 ~~[[48]]~~, wherein the engineered structural formation is one of a surface groove and a passageway within the membrane.

50. (Withdrawn) The substrate of claim 49, wherein the surface groove or passageway within the membrane has a diameter of less than 100μ .
51. (Withdrawn) The substrate of claim 49, wherein the membrane comprises an internal passageway that opens into the interior volume.
52. (Withdrawn) The substrate of claim 51, wherein the passageway is coated with an extracellular matrix mimetic.
53. (Withdrawn) The substrate of claim 31, wherein the elastomeric membrane is biodegradable.
54. (Withdrawn) The substrate of claim 53, wherein the biodegradable membrane comprises a poly(glycerol-sebacate) polymer.
55. (Withdrawn) The substrate of claim 31, wherein at least a portion of the substrate is coated with an adhesion promoter.
56. (Currently amended) A cell growth apparatus comprising a cell growth chamber having an interior side and an exterior side and comprising a wall and a base defining an interior volume, the cell growth chamber comprising an elastomeric growth substrate comprising an elastomeric membrane of a first material having an interior side and an exterior side, wherein the elastomeric membrane is at least partially coated with an extracellular matrix-mimetic, the elastomeric membrane having one or more engineered structural formations integrated therewith for receiving and growing cells.
57. (Original) The apparatus of claim 56, wherein the membrane comprises a first portion having a first elasticity and a second portion having a second elasticity.
58. (Original) The apparatus of claim 56, wherein at least a portion of the base of the cell growth chamber consists of the elastomeric growth substrate.

59. (Original) The apparatus of claim 58, further comprising a secondary chamber in fluid connection with and partially defined by an exterior side of the elastomeric growth substrate, the secondary chamber comprising an opening having a fitting for a pipe or tube.
60. (Original) The apparatus of claim 59, further comprising a pump in fluid communication with the secondary chamber.
61. (Original) The apparatus of claim 56, wherein the elastomeric membrane has a portion of a first thickness, having a first elasticity, and a portion of a second thickness, having a second elasticity.
62. (Original) The apparatus of claim 56, wherein a second material having a different elasticity than the first material is embedded within or attached to the elastomeric membrane.
63. (Original) The apparatus of claim 62, wherein the second material is one of a polymer, a metal, a ceramic and a fabric.
64. (Original) The apparatus of claim 63, wherein the second material is a nylon mesh.
65. (Original) The apparatus of claim 63, wherein the second material is a stainless steel mesh.
66. (Original) The apparatus of claim 56, wherein the substrate further comprises one or more additional elastomeric layers, at least one of which is attached to the elastomeric membrane.
67. (Original) The apparatus of claim 66, wherein one or more of the additional elastomeric layer is biodegradable.
68. (Original) The apparatus of claim 67, wherein the biodegradable layer comprises a poly(glycerol-sebacate) polymer.

69. (Original) The apparatus of claim 56, wherein the extracellular matrix mimetic is selected from the group consisting of fibronectin, vitronectin, collagen, laminin, poly(lactide), poly(lactide-co-glycolide) and a self-complementary oligopeptide matrix.
70. (Original) The apparatus of claim 69, where in the extracellular matrix mimetic is fibronectin.
71. (Original) The apparatus of claim 56 wherein the first portion has a first elastic modulus and the second portion has a second elastic modulus.
72. (Original) The apparatus of claim 56, wherein the membrane comprises one or more internal passageways.
73. Cancelled
74. (Currently amended) The apparatus of claim 56 [[73]], wherein the engineered structural formation is one of a surface groove and a passageway within the membrane.
75. (Original) The apparatus of claim 74, wherein the surface groove or passageway within the membrane has a diameter of less than 100 μ .
76. (Original) The apparatus of claim 75, wherein the membrane comprises an internal passageway that opens into the interior volume.
77. (Original) The apparatus of claim 76, wherein the passageway is coated with an extracellular matrix mimetic.
78. (Original) The apparatus of claim 56, wherein the extracellular matrix mimetic partially coats the interior side of the elastomeric membrane.
79. (Original) The apparatus of claim 78, further comprising a adhesion inhibitor covering parts of the interior side of the elastomeric membrane not covered by the extracellular matrix mimetic.

80. (Original) The apparatus of claim 79, wherein the adhesion inhibitor is one of bovine serum albumin and a poly(ethylene oxide)/poly(propylene oxide)/poly(ethylene oxide) triblock polymer.
81. (Original) The apparatus of claim 56, wherein the elastomeric membrane is biodegradable.
82. (Original) The apparatus of claim 81, wherein the biodegradable membrane comprises a poly(glycerol-sebacate) polymer.
83. (Original) The apparatus of claim 56, wherein the wall is annular.
84. (Original) The apparatus of claim 56, wherein the wall is ellipsoid.
85. (Original) The apparatus of claim 56, wherein at least a portion of the substrate is coated with an adhesion promoter.
86. (Currently amended) A cell growth substrate, comprising an elastomeric membrane of a first material that is at least partially coated with an extracellular matrix-mimetic, the elastomeric membrane defining a three-dimensional cell strain surface having an elasticity differential that comprises one of (i) an elastic modulus differential between a first portion and a second portion of the first material and (ii) a surface feature differential between the first and second portions, the elastomeric membrane having one or more engineered structural formations integrated therewith for receiving and growing cells.
87. Cancelled.
88. (Original) The substrate of claim 86, wherein the elastomeric membrane has a portion of a first thickness, having a first elasticity, and a portion of a second thickness, having a second elasticity.
89. (Original) The substrate of claim 86, wherein a second material having a different elasticity than the first material is embedded within or attached to the elastomeric membrane.

90. (Original) The substrate of claim 89, wherein the second material is one of a polymer, a metal, a ceramic and a fabric.
91. (Original) The substrate of claim 90, wherein the second material is a nylon mesh.
92. (Original) The substrate of claim 90, wherein the second material is a stainless steel mesh.
93. (Original) The substrate of claim 86, wherein the substrate further comprises one or more additional elastomeric layers, at least one of which is attached to the elastomeric membrane.
94. (Original) The substrate of claim 93, wherein one or more of the additional elastomeric layer is biodegradable.
95. (Original) The substrate of claim 94, wherein the biodegradable layer comprises a poly(glycerol-sebacate) polymer.
96. (Original) The substrate of claim 86, wherein the extracellular matrix mimetic is selected from the group consisting of fibronectin, vitronectin, collagen, laminin, poly(lactide) , poly(lactide-co-glycolide) and a self-complementary oligopeptide matrix.
97. (Original) The substrate of claim 96, where in the extracellular matrix mimetic is fibronectin.
98. (Original) The substrate of claim 86, wherein the first portion has a first elastic modulus and the second portion has a second elastic modulus.
99. (Original) The substrate of claim 86, wherein the membrane comprises one or more internal passageways.
100. Cancelled.

101. (Currently amended) The substrate of claim 86 ~~[[100]]~~, wherein the engineered structural formation is one of a surface groove and a passageway within the membrane.

102. (Original) The substrate of claim 101, wherein the surface groove or passageway within the membrane has a diameter of less than 100 μ .

103. (Original) The substrate of claim 101, wherein the membrane comprises an internal passageway that opens into the interior volume.

104. (Original) The substrate of claim 103, wherein the passageway is coated with an extracellular matrix mimetic.

105. (Original) The substrate of claim 86, wherein the extracellular matrix mimetic partially coats the interior side of the elastomeric membrane.

106. (Original) The substrate of claim 105, further comprising an adhesion inhibitor agent covering parts of the interior side of the elastomeric membrane not covered by the extracellular matrix mimetic.

107. (Original) The substrate of claim 106, wherein the adhesion inhibitor is one of bovine serum albumin and a poly(ethylene oxide)/poly(propylene oxide)/poly(ethylene oxide) triblock polymer.

108. (Original) The substrate of claim 86, wherein the elastomeric membrane is biodegradable.

109. (Original) The substrate of claim 108, wherein the biodegradable membrane comprises a poly(glycerol-sebacate) polymer.

110. (Original) The apparatus of claim 86, wherein at least a portion of the substrate is coated with an adhesion promoter.

111. (Currently amended) A method of producing an elastomeric cell growth substrate, comprising integrating one or more engineered structural formations with an elastomeric

membrane, and coating at least a portion of ~~[[an]]~~ the elastomeric membrane with an extracellular matrix mimetic.

112. (Original) The method of claim 111, wherein the extracellular matrix mimetic is selected from the group consisting of fibronectin, vitronectin, collagen, laminin, poly(lactide), poly(lactide-co-glycolide) and a self-complementary oligopeptide matrix.

113. (Original) The method of claim 111, where in the extracellular matrix mimetic is fibronectin.

114. (Original) The method of claim 111, further comprising coating at least a portion of the elastomeric membrane with an adhesion inhibitor.

115. (Original) The method of claim 114, wherein the adhesion inhibitor is bovine serum albumin.

116. (Original) The method of claim 114, wherein the adhesion inhibitor is a poly(ethylene oxide)/poly(propylene oxide)/poly(ethylene oxide) triblock polymer.

117. (Original) The method of claim 111, wherein the membrane has a first portion having a first elasticity and a second portion having a second elasticity.

118. (Original) The method of claim 117, wherein the first portion has a first elastic modulus and the second portion has a second elastic modulus.

119. (Original) The method of claim 117, wherein the membrane has portions of differing thickness.

120. (Original) The method of claim 117, wherein a material of a different elastic modulus than that of the membrane is embedded within or attached to the membrane.

121. (Original) The method of claim 120, wherein the material is one of a nylon mesh and a stainless steel mesh.

122. (Original) The method of claim 117, wherein the membrane comprises one or more internal passageways.
123. Cancelled.
124. (Currently amended) The method of claim 111 ~~[[123]]~~, wherein the engineered structural formation is one of a surface groove and a passageway within the membrane.
125. (Original) The method of claim 124, wherein the surface groove or passageway within the membrane has a diameter of less than 100 μ .
126. (Currently amended) The method of claim 111 ~~[[123]]~~, wherein the membrane is prepared by curing an elastomeric polymer in a mold containing a form defining the engineered structural formation.
127. (Original) The method of claim 126, wherein the form defining the engineered structural formation is a silicon wafer comprising a patterned photoresist layer defining the engineered structural formation.
128. (Original) The method of claim 126, comprising pouring PDMS over a silicon wafer comprising a patterned photoresist layer defining the engineered structural formation and heat curing the PDMS.
129. (Original) The method of claim 126, wherein the engineered structural formation is a channel.
130. (Currently amended) The method of claim 111 ~~[[123]]~~, wherein a second elastomeric layer is attached to the membrane.
131. (Original) The method of claim 130, wherein the engineered structural formation is a groove and the second elastomeric layer is aligned over the groove to form a passageway.
132. (Withdrawn and currently amended) A method of producing an elastomeric cell growth substrate, comprising, preparing an elastomeric membrane of a first material that comprises a

first portion having a first elasticity and a second portion having a second elasticity, and integrating one or more engineered structural formations with an elastomeric membrane.

133. (Original) The method of claim 132, comprising coating at least a portion of the elastomeric membrane with an extracellular matrix mimetic.

134. (Withdrawn) The method of claim 132, wherein the extracellular matrix mimetic is selected from the group consisting of fibronectin, vitronectin, collagen, laminin, poly(lactide), poly(lactide-co-glycolide) and a self-complementary oligopeptide matrix.

135. (Original) The method of claim 133, where in the extracellular matrix mimetic is fibronectin.

136. (Withdrawn) The method of claim 132, further comprising coating at least a portion of the elastomeric membrane with an adhesion inhibitor.

137. (Withdrawn) The method of claim 136, wherein the adhesion inhibitor is bovine serum albumin.

138. (Withdrawn) The method of claim 136, wherein the adhesion inhibitor is a poly(ethylene oxide)/poly(propylene oxide)/poly(ethylene oxide) triblock polymer.

139. (Withdrawn) The method of claim 132, wherein the first portion has a first elastic modulus and the second portion has a second elastic modulus.

140. (Withdrawn) The method of claim 132, wherein the membrane has portions of differing thickness.

141. (Withdrawn) The method of claim 132, wherein a material of a different elastic modulus than that of the membrane is embedded within or attached to the membrane.

142. (Withdrawn) The method of claim 141, wherein the material is one of a nylon mesh and a stainless steel mesh.

143. (Withdrawn) The method of claim 132, wherein the membrane comprises one or more internal passageways.

144. Cancelled.

145. (Withdrawn and currently amended) The method of claim 132 ~~[[144]]~~, wherein the engineered structural formation is one of a surface groove and a passageway within the membrane.

146. (Withdrawn) The method of claim 145, wherein the surface groove or passageway within the membrane has a diameter of less than 100μ .

147. (Withdrawn and currently amended) The method of claim 132 ~~[[144]]~~, wherein the membrane is prepared by curing an elastomeric polymer in a mold containing a form defining the engineered structural formation.

148. (Withdrawn) The method of claim 147, wherein the form defining the engineered structural formation is a silicon wafer comprising a patterned photoresist layer defining the engineered structural formation.

149. (Withdrawn) The method of claim 147, comprising pouring PDMS over a silicon wafer comprising a patterned photoresist layer defining the engineered structural formation and heat curing the PDMS.

150. (Withdrawn) The method of claim 147, wherein the engineered structural formation is a channel.

151. (Withdrawn and currently amended) The method of claim 132 ~~[[144]]~~, wherein a second elastomeric layer is attached to the membrane.

152. (Withdrawn) The method of claim 151, wherein the engineered structural formation is a groove and the second elastomeric layer is aligned over the groove to form a passageway.

153. (Withdrawn and currently amended) A method of culturing cells, comprising:

(a) growing cells in a suitable cell growth medium in a cell growth apparatus comprising a cell growth chamber having an interior side and an exterior side and comprising a wall and a base defining an interior volume, the cell growth chamber comprising an elastomeric growth substrate comprising an elastomeric membrane of a first material that comprises a first portion having a first elasticity and a second portion having a second elasticity, the elastomeric membrane having one or more engineered structural formations integrated therewith for receiving the cells; and

(b) flexing the ~~substrate~~ elastomeric membrane while the cells are growing.

154. (Withdrawn) The method of claim 153, further comprising adding an analyte to the cell culture and determining the effect of the analyte on the cells.

155. (Withdrawn and currently amended) A method of culturing cells, comprising:

(a) growing cells in a suitable medium in a cell growth apparatus comprising a cell growth chamber having an interior side and an exterior side and comprising a wall and a base defining an interior volume, the cell growth chamber comprising an elastomeric growth substrate comprising an elastomeric membrane of a first material that is at least partially coated with an extracellular matrix-mimetic, the elastomeric membrane having one or more engineered structural formations integrated therewith for receiving the cells; and

(b) flexing the substrate while the cells are growing.

156. (Withdrawn) The method of claim 155, further comprising adding an analyte to the cell culture and determining the effect of the analyte on the cells.

157. (Withdrawn) A method of culturing cells, comprising:

(a) growing cells in a suitable cell growth medium in a cell growth apparatus comprising a cell growth chamber having an interior side and an exterior side and comprising a wall and a base defining an interior volume, the cell growth chamber comprising an elastomeric growth substrate comprising a first elastomeric membrane and a removable second elastomeric

membrane having one or more protuberances contacting the first elastomeric membrane or one or more openings, the periphery of which contact the first elastomeric membrane;

- (b) flexing the substrate while the cells are growing; and
- (c) removing the second elastomeric membrane.